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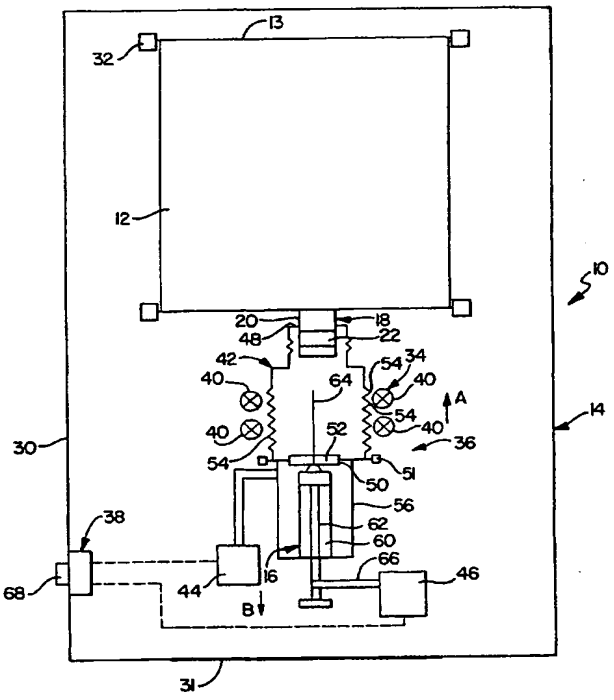
(54) Title: MULTI-DOSE CONTAINER SYSTEM



(57) Abstract: The present invention provides a multi-dose container system (10) for withdrawing multiple doses of a drug solution from the system over an extended period of time. The system has a container (12) having a port assembly (18) extending from the container (10). The port assembly (18) has a port tube (20) sealed by a stopper (22). The container (10) holds a drug solution. A bellows assembly (42) has a first end opening (48) positioned over the port assembly (18) and a second end opening (50) sealed by a septum (52). The bellows assembly (42) is movable between a first position and a second, collapsed position. A sterilization device (14) is positioned adjacent the bellows assembly (42) and is adapted to sterilize a needle (64) placed in the bellows assembly (42). A syringe assembly (16) has a syringe barrel (60) with a needle (64) at one end and a plunger (62) slidable within the syringe barrel (60). A syringe activator (44) is connected to the syringe assembly (16) for moving the syringe assembly (16) and for moving the bellows assembly (42) from the first position to the second position. A plunger activator (46) has an arm (66) connected to the plunger (62). The syringe activator (44) moves the syringe assembly (16) wherein the needle (64) pierces the septum (52) and is positioned within the bellows assembly (42). After the sterilization device (14) sterilizes the needle (64), the syringe activator (44) moves the bellows assembly (42) to the collapsed position wherein the needle (64) pierces into the port assembly (18). The plunger activator (46) then pulls back on the plunger (62) withdrawing drug solution from the container (12) into the syringe barrel (60).

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MULTI-DOSE CONTAINER SYSTEM

DESCRIPTION

Related Application

The present invention claims the benefit of U.S. Provisional Patent Application No. 60/242,209, filed on October 20, 2000, entitled "Multi-Dose Container System," which application is expressly incorporated herein by reference.

Technical Field

The present invention relates generally to a system for the delivery of a sterile, flowable medicament. More specifically, the present invention relates to a medical container system having a container storing a drug solution that allows for multiple doses of the drug solution to be withdrawn in a controlled manner over an extended period of time while preventing entry of external contaminants during and between withdrawals.

Background of the Invention

In certain medical applications, a doctor may treat a patient periodically with the same drug. Also, in hospital pharmacies, a pharmacist may be required to prepare several doses of the same drug over an extended period of time.

In one hospital pharmacy practice, a pharmacist may prepare an intravenous drug solution. Rather than preparing the solution for storage in a bulk container for later withdrawals, the pharmacist aliquots portions of the entire solution into unit of use containers, e.g. syringes, which are then stored appropriately, and removed as needed. In oncology pharmacy practice, however, drug dosages are often required in non-standard amounts because the dosages are determined based on individual parameters of each patient. In this case, prior preparation of dosages is not feasible because of uncertainty as to which dosage should be

prepared. Furthermore, current oncology pharmacy practice entails reconstitution of a drug in a vial with diluent, withdrawal of the appropriate volume for a given patient, and discarding the remaining contents of the vial if the contents are not used within the prescribed period of time after reconstitution. This inevitably leads to drug wastage.

Therefore, in oncology pharmacy practice and in similar situations, it is desirable to have a drug container, containing multiple doses of a drug, that can be repeatedly accessed over a period of time to withdraw individual, variable, doses of the drug to be delivered to the patient. The drug container that contains multiple doses of a drug is sometimes referred to as a "mother container."

Current United States Pharmacopeia (U.S.P.) guidelines stipulate that only two systems can be used to provide a mother container that can be repeatedly accessed over a period of time. One system is termed a pharmacy bulk pack container system. This system provides a bulk pack container containing a drug solution. Once this mother container is entered, however, it must be discarded after four hours. If all of the drug solution has not been used, it must be discarded as well. In another system, a mother container is provided containing a drug solution having a bacterial preservative. This multi-dose container permits repeated entry over a much longer period. The presence of the bacterial preservative in the drug solution, however, severely restricts the ability to use such a container with a variety of drugs. In addition, the drug manufacturer is required to show that the bacterial preservative does not have an adverse impact on the drug solution.

Another system is used in blood banking for repeatedly transferring blood components from storage to administration containers in a sterile manner. In this system, a mother container holding blood has a closed plastic tube at one end. A sterile empty container also having a closed plastic tube is provided to be filled with blood from the mother container. This container is sometimes called the "daughter container." The plastic tubes from the mother container and daughter container are joined together using a Food and Drug Administration (FDA) approved sterile connector device known in the marketplace as the Terumo Sterile Connector Device. The tubes of the containers are brought together, side by side, in the Sterile Connector Device. The Sterile Connector Device is equipped with a heat sterilized metal blade that is actuated to sever the tubes aseptically. The tubes are then moved relative to one another aligning their open ends wherein the hot ends of the tubes are welded together. This provides a sterile connection

and fluid flow path between the mother container and daughter container. The desired amount of blood is then transferred from the mother container to the daughter container. The Sterile Connector Device is activated again to cut the umbilical tubing joining the two containers and to seal both ends of the severed tubing. While this procedure is adequate for blood transfer, it is generally not used in hospital pharmacy practice because it can be slow and requires a number of manipulations.

It is apparent that dispensing multiple doses of a drug solution from a container over a prolonged period of time in a contamination-free manner presents several issues. Oftentimes, one cannot assume that a needle remains sterilized just before it is inserted into a mother container. Thus, there remains the potential for the entire contents of a drug solution contained in a mother container to become contaminated. Subsequent aliquots withdrawn from such a system could result in microbial infection if injected into patients. Generally speaking, it is difficult to overcome the limitations of conventional syringe/needle technology used with mother containers over an extended period of time and maintain a sterile process.

Thus, there still remains a need for providing a multi-dose container system that allows for multiple doses of a drug to be withdrawn in a sterile manner over a prolonged period of time.

Also, in a hospital pharmacy, especially when preparing oncology drugs, the pharmacist can be exposed to dangerous aerosols which are released when the drugs are withdrawn from standard glass vials. When the drugs are reconstituted in the vials, pressure builds up in the glass vial creating a pressure differential between the container interior and ambient conditions. When a needle is inserted into a rubber stopper of the vial to withdraw the reconstituted drug, pressure escapes between the needle exterior and rubber stopper. Accordingly, there also remains a need for a system that can protect a user from these dangerous aerosols.

Additional problems are encountered in accessing other types of containers in a sterile fashion. These containers include, but are not limited to, cell culture containers, blood containers, various other types of drug containers, and food containers. The containers can also include drug, chemical, and biofermentation reactors. Opening these containers for the addition of ingredients, or the withdrawal of quality control samples, creates a risk of contamination.

The present invention is provided to solve these and other problems.

Summary Of The Invention

The present invention provides a multi-dose container system for withdrawing multiple doses of a flowable material from the system over an extended period of time. The system has a container having a port assembly extending from the container. The port assembly has a tube sealed by a plug. The container holds a flowable material. A bellows assembly has a first end opening positioned over the port assembly and a second end opening sealed by a septum. The bellows assembly is movable between a first position and a second, collapsed position. A sterilization device is positioned adjacent the bellows assembly and is adapted to sterilize a needle placed in the bellows assembly. A syringe assembly has a syringe barrel with a needle at one end and a plunger slidable within the syringe barrel. A syringe activator is connected to the syringe assembly for moving the syringe assembly and for moving the bellows assembly from the first position to the second position. A plunger activator has an arm connected to the plunger. The syringe activator moves the syringe assembly wherein the needle pierces the septum and is positioned within the bellows assembly. After the sterilization device sterilizes the needle, the syringe activator moves the bellows assembly to the collapsed position wherein the needle pierces into the port assembly. The plunger activator then pulls back on the plunger withdrawing material from the container into the syringe barrel.

According to another aspect of the invention, the sterilization device may comprise UV sterilization. Other sterilization methods are also possible such as heat sterilization, chemical sterilization and radiation.

According to a further aspect of the invention, the process of withdrawing a specific dosage of a drug solution from the container is automated.

Other aspects of the invention will be apparent from the following specification taken in conjunction with the following drawings.

Brief Description Of The Drawings

FIG. 1 is a plan view of the multi-dose container system of the present invention; and

FIG. 2 is a schematic diagram of a process for obtaining a drug dose from the multi-dose container system of the present invention.

Detailed Description of the Preferred Embodiments

While the invention is susceptible of embodiment in many different forms, there is shown in the drawings and will herein be described in detail preferred embodiments of the invention. It is to be understood that the present disclosure is to be considered as an exemplification of the principles of the invention. This disclosure is not intended to limit the broad aspect of the invention to the illustrated embodiments.

The present invention provides a multi-dose container system allowing for withdrawal of multiple doses of a drug over an extended period of time. Referring to the Figures, FIG. 1 discloses a multi-dose container system generally designated with the reference numeral 10. The multi-dose container system 10 generally includes a container 12, a dispensing/sterilization device 14, and a syringe assembly 16. The components of the multi-dose container system 10 are designed to resist the accumulation of contaminants on their surfaces and are made from materials that are compatible with cleaning solvents used by hospital pharmacies.

The container 12 is preferably a flexible container made from any number of plastic films known in the art. The container material will be selected to be compatible with the drug solution contained. The container 12 is sized to hold multiple doses of a drug in solution form. The container 12 could be sized in the range of a 50 ml container to a one liter container. In one preferred embodiment, the container 12 holds 6 to 10 doses of the drug solution. The container 12 has a port assembly 18 that is adapted to receive a needle from the syringe assembly 16. The port assembly 18 has a port tube 20 that extends from sidewalls of the container 12. The port tube 20 is closed by a resilient rubber stopper 22 that is inserted into the port tube 20. In a preferred embodiment, the solution contacting layer of the port tube 20, along with the container 12, is PVC-free such as a polyolefin material as this material displays the desired inert characteristics. In another preferred embodiment, the port tube 20 is non-DEHP PVC, along with the container 12. Nevertheless, it is also possible to use PVC material. The rubber stopper 22 is designed so that it can be pierced multiple times without affecting the integrity of the stopper 22 and causing unwanted leaking.

The container 12 can be filled with the drug solution at a drug manufacturing site using terminal sterilization or aseptic filling techniques, or it could be shipped as a sterile, empty container, permitting, for example, the hospital pharmacy the flexibility to use the container for any admixture desired and prepared in the pharmacy. While a flexible container 12 is preferred,

a rigid container, such as a glass container, could also be used. A rigid container would be fitted with a venting, antimicrobial filter to accommodate the pressure differential generated upon withdrawing the drug solution.

FIG. 1 also discloses the dispensing/sterilization device 14. The dispensing/sterilization device 14 generally includes a housing 30, a container support 32, sterilization assembly 34, a syringe autoholder mechanism 36 and a control mechanism 38. The housing 30 is a rigid structure and is sized to hold all of the components of the system 10 including the multi-dose container 12. In a preferred embodiment, however, the entire system is sized such that the individual components can be placed in a laminar flow hood, for example, in a hospital pharmacy. In such case, the housing 30 is not used. In some applications where drug compounding is necessary, a laminar flow hood is not available such as at a hospital nursing station. In such case, the housing 30 would be used to contain the system components. As further shown in FIG. 1, the container support 32 is connected to the container 12 and is adapted to lift an end 13 of the bag opposite the port assembly 18 to assure that when the syringe assembly 16 is inserted into the port assembly 18 for withdrawal, the port assembly 18, at the interior of the container 12, is completely surrounded by solution. Alternatively, a clamp could be provided to grip the port tube 20, to rotate the port assembly 18 to ensure the port assembly 18 is completely surrounded by solution at the interior of the container 12.

FIG. 1 further shows the sterilization assembly 34. The sterilization assembly 34 is an ultra-violet sterilization device having a plurality of annular-shaped lamps 40 that will be described in greater detail below. As further detailed below, in one preferred embodiment, UV sterilization is used, but other sterilization methods can also be used in the present invention such as heat sterilization, chemical sterilization and radiation.

FIG. 1 also shows the syringe autoholder mechanism 36. The mechanism 36 includes a collapsible member or bellows assembly 42, a syringe activator 44, and a plunger activator 46. The bellows assembly 42 has a first end opening 48 opposing a second end opening 50. The first end opening 48 sealingly fits around the port assembly 18. The second end opening 50 is sealed by a septum 52. In a preferred embodiment, the septum 52 is made from silicone rubber and is impregnated with an antimicrobial additive such as hydrogen peroxide. The bellows assembly 42 further has a plurality of bellows 54 along its length. The bellows assembly 42 can be constructed from LLDPE material in a blow-molding process. Before the bellows assembly

42 is installed within the housing 30, a cap (not shown) may be fitted over the septum 52, which must be removed before system operation. The autoholder mechanism 36 further has a carriage 56 to support the syringe assembly 16. The carriage 56 is adapted to connect to the bellows assembly 42 during the withdrawal process as described below. The syringe activator 44 is connected to the carriage 56 and moves the carriage 56 and can contract and expand the bellows assembly 42 as described in greater detail below. In a preferred embodiment, the bellows assembly 42 provides an enclosed, controlled area where the sterilization procedure can be completed. It is understood, however, that the sterilization procedure can be completed without utilizing the bellows assembly 42.

FIG. 1 further shows a plunger activator 46. The syringe assembly 16 has a barrel 60 with a plunger 62 slidable within the barrel 50. The syringe assembly 16 further has a piercing member in the form of a needle 64. The needle length is sized appropriately so it does not pierce completely through the container 12. The plunger activator 46 has an arm 66 that connects to the plunger 62. The syringe assembly 16 is designed to resist the accumulation of contaminants on its surface and is made from materials that are compatible with cleaning solvents used by hospital pharmacies. It is understood that the syringe assembly 16 is merely a second container used in the system 10 and can also take other forms.

The control mechanism 38 is electrically connected to the syringe activator 44 and the plunger activator 46. The control mechanism 38 has a push button 68 mounted on an exterior surface of the housing 30. The push button 68 will activate an automatic process as described below. As will be described below, the control mechanism 38 has the capacity to control the entire system 10 and can receive data inputted by an operator before a withdrawal process is commenced. For example, certain data can be pre-programmed into the mechanism 38 such as the desired dosage to be withdrawn from the container 12, patient ID, drug name, concentration, volume, bar code and related information. As explained below, all of this information could be printed on a label to be applied to the syringe assembly 16.

The multi-dose container system 10 can be set-up in a hospital pharmacy such as in a laminar flow hood. As discussed, if the system 10 is placed in a hood, it typically would not utilize a housing 30. The pharmacy may have several systems 10 holding different drug solutions. Depending on the drug contained in the container, the containers 12 may be refrigerated or stored at room temperature. Referring to FIGS. 1 and 2, in practice, the multi-

dose container system 10 is first set-up. An operator, such as a hospital pharmacist, selects a container 12 containing the drug solution of interest. The pharmacist then docks the container 12 to the dispensing/sterilization device 14. To this end, the pharmacist first connects the container 12 to the container support 32, or if a clamp is used with the port assembly 18, to the clamp. In an application not utilizing a hood, the pharmacist would place the container 12 in the housing 30 through an appropriate access door 31 on the housing 30. The autoholder 36 is connected to the container wherein the bellows assembly 48 has its first end opening 42 sealingly attached over the port assembly 18 of the container 12. The UV sterilization device 34 is positioned around the bellows assembly 42. In a preferred embodiment, the lamps 40 of the sterilization device 34 are annular in shape and extend completely around the bellows assembly 42 to, therefore, assure complete sterilization around the needle 64. In an alternative embodiment, the bellows assembly 42 can be designed to house the sterilization device 34 within the bellows assembly 42. If the sterilization device 34 is positioned outside of the bellows assembly 42, it is assured that the wavelength of the light emitted from the device 34 is sufficient to pass through the material of the bellows assembly 42 to assure sterilization of the needle 64 can be accomplished.

The pharmacist determines the drug dosage called for and selects a syringe assembly 16 of an appropriate size. The system 10 can accommodate syringe assemblies 16 of varying sizes, e.g., from a 1cc syringe assembly to a 60 ml syringe assembly. The needle 64 of the syringe assembly 16 is placed onto the syringe barrel 60 and is removable. The syringe assembly 16 is then docked to the dispensing/sterilization assembly 14 and, in particular, to the autoholder 36. The syringe assembly 16 is placed in the carriage 56. It is noted that FIG. 1 shows the needle 64 already pierced through the septum 52 wherein the needle 64 is within the bellows assembly 42 and adjacent the UV lamps 40. It is understood, however, that upon initial set-up, the needle 64 is positioned outside the bellows assembly 42 and adjacent the septum 52. The syringe activator 44 is connected to the carriage 56 and the arm 66 of the plunger activator 46 is connected to the syringe plunger 62. The pharmacist then confirms that the proper dosage has been programmed into the control system 38 and the proper container 12 has been selected. The system 10 is now ready for activation.

The pharmacist activates the control system 38 by depressing the push button 68. The control system 38 then controls the system 10 in the following manner. The container support

32 tilts an end of the container 12 to assure solution covers the port assembly 18. This could be done later in the process but just before the needle 64 is inserted into the port assembly 18. The syringe activator 44 is activated to move the syringe assembly 16 towards the container 12 wherein the needle 64 pierces through the septum 52 and into the bellows assembly 42. This movement can be closely controlled such that the needle 64 can adequately contact the antimicrobial additives in the septum 52. Bellows supports 51 act to support the bellows assembly 42 so the needle 64 can pierce through the septum 52. The carriage 56 abuts the bellows assembly 42 and the system 10 assures that the needle 64 is stationary with the bellows assembly 42. The UV sterilization system 34 is activated wherein the lamps 40 emit ultraviolet light to sterilize the needle 64 and the entire volume inside the bellows assembly 42. It is further noted that the surface of the stopper 22 and surface of the septum 52 facing into the bellows assembly 42 are also sterilized. Once the proper time has elapsed to assure that all surfaces including the needle 64 have been sterilized, the lamps 40 are shut off. The control system 38 then again activates the syringe activator 44. The syringe activator 44 extends further towards the container 12 to collapse the bellows 54, thus advancing the syringe assembly 16 towards the port assembly 18 (Arrow A). The bellows 54 further collapse wherein the needle 64 pierces the rubber stopper 22 and enters the container 12. The syringe activator 42 is deactivated. It is understood that the plunger activator 46 is designed to move with the syringe activator 44. The plunger activator 46 is then activated wherein the arm 66 pulls back on the plunger 62 (Arrow B). Thus, drug solution is withdrawn from the container 12 and into the syringe barrel 60. As stated, prior to system activation, the control system is programmed for the correct dosage to be withdrawn and, therefore, determines how far the plunger 62 is to be pulled back. Once the correct dosage is withdrawn, the plunger activator 46 is deactivated. The syringe activator 44 is then activated to expand the bellows 54 and pull the syringe assembly 16 out of the container 12. The syringe activator 44 further pulls the syringe assembly 16 out of the bellows assembly 42 with the proper structure present to allow the needle 64 to be pulled from the septum 52. The rubber stopper 22 and septum 52 are designed such that they reseal once the needle 64 is pulled out. The withdrawal of the syringe assembly 16 is controlled to assure that the bellows assembly 42 does not expand too quickly to move further back on the needle 64 wherein portions of the needle 64 towards the barrel end that may have not been sterilized could be moved into the bellows assembly 42. With the syringe

assembly 16 removed from the bellows assembly 42, an automatic process may install a needle cover (not shown) over the needle 64.

At this time, the withdrawal process complete. The control system 38 may be equipped with an alarm to alert the pharmacist that the syringe assembly 16 can now be removed from the system 10. The pharmacist disconnects the arm 66 from the plunger 62 and pulls the syringe assembly 16 out of the bellows assembly 42. If desired, the needle 64 can be removed from the syringe assembly 16 and another needle (not shown) can be inserted onto the syringe assembly 16. The new needle will be used to inject the drug solution into a patient. Because the needle 64 has been in a sterile environment throughout the complete process, the needle 64 can be used with the patient if desired. The pharmacist then delivers the syringe assembly 16 to the appropriate location for medical personnel to inject the drug solution into a patient. The container system 10 may then be set-up for another withdrawal or stored appropriately if another dose is not required until a later time.

It is understood that the benefits of the present invention can be realized without the use of the bellows assembly 42. The bellows assembly 42, however, allows the withdrawal process to be completed with a single sterilization step.

Other features can be incorporated into the system 10 if desired. The process can also be further automated. For example, a syringe magazine could be included in the system and designed to hold several syringes that could be fed into the autoholder 36 to be filled. In addition, it is also contemplated that several syringe magazines could be included in the system 10 and designed to hold a plurality of different sized syringes that could feed appropriately sized syringe assemblies to the autoholder 36 for filling with an appropriate dosage. Thus, the appropriate size syringe, based on the programming of the control system 38, could automatically be placed in the autoholder 36 when the sequence is initially activated. This automation would also be beneficial when filling several identical volumes in syringes, such as for flush solutions. The system 10 could also be equipped with an automatic print-out of dosages prepared. To reduce medical errors, an autolabeling feature (e.g., identifying patient, dosage, drug name, concentration, volume, time, bar coding and related information etc.) could be incorporated to automatically print the label and affix it to the syringe. A remote ordering feature could also be incorporated. Patient data can also be programmed into the system 10.

In an alternative embodiment, the sterilization assembly 34 can be a heat sterilization device. The heat sterilization device could be housed within the bellows assembly 42. Before piercing into the port assembly 18, the needle 64 is first dry heat sterilized for the appropriate time required to achieve sterilization. The needle 64 is subjected to a hot air blast greater than 350 °C. In this embodiment, the needle length is selected such that the portion of the needle 64 closest to the syringe barrel is insulated by the length of the needle so that the plastic hub that typically supports the needle on the syringe barrel is not melted. A heat sink could be added to keep the needle hub cool. Following exposure of the needle 64 to the requisite temperature and duration of time appropriate to assure sterilization, the needle 64 is rapidly cooled to avoid incurring stability issues or chemical compatibility issues with the drug solution held by the container 12. The needle 64 is cooled by cold air blasts, typically to room temperature if the container 12 is stored at room temperature. The needle 64 is then inserted into the port assembly 18 of the container 12. In this application, the rubber stopper 22 is designed to have a certain amount of heat resistance. An appropriate dosage of the drug solution is then withdrawn from the container 12 as described above. It is understood that the heat sterilization device could be used with or without a bellows assembly.

Other sterilization processes could also be used. For example, the needle 64 could be chemically sterilized provided issues relating to chemical interaction with the drug solution are addressed. Chemical sterilization could be accomplished by using a gas or liquid medium. Gas mediums include ethylene oxide, propylene oxide, chlorine dioxide, formaldehyde, hydrogen peroxide, peracetic acid, ozone, chloropicrin, and methyl bromide. Other dry heat sterilization procedures could also be used including radio-frequency, microwave, and direct conductive processes. Radiation such as radio-frequency induction, microwave radiation, electromagnetic radiation or particle radiation can be used. Electromagnetic radiation can include UV, gamma and X-radiation. Particle radiation can include beta radiation. Induction heating could also be used wherein dry heat or wet heat is delivered by contact with a hot surface. Hot gas could also be used. In another embodiment, a flame could be used to heat and sterilize the needle.

A heating device could also be directly connected to the syringe assembly 16 to heat the needle 64. In this application, electric current could be directly passed through the needle 64 to heat the needle 64. The current is controlled to evenly heat the needle to a temperature sufficient to sterilize the needle 64. A heated contact block could also be utilized wherein the

needle 64 would be placed in contact with the contact block before insertion into the port assembly 18. This could be done very efficiently because the contact block can be preheated wherein the needle would be heated very quickly. This method is also very simple. Laser diode technology could also be used as a source of UV light for sterilization purposes.

The multi-dose container system 10 of the present invention provides several advantages. First, repeated sterile access to the container 12 is assured because the needle 64 is sterilized immediately before each insertion into the container 12. Accordingly, an antimicrobial preservative is not necessary. This is beneficial because there is now no need to prove that the antimicrobial preservative will not have an adverse effect on the drug solution itself. Furthermore, repeated sterile access is also allowed over extended periods of time, far in excess of the current four hour period allowed. At the same time, with the present system a pharmacist also enjoys the efficiencies of standard pharmacy automation. For example, with the automated features of the present invention, the pharmacist can activate the fill procedure, attend to other matters, and return to obtain a properly filled and labeled syringe when the procedure is complete. The procedure can be repeated over an extended period of time, e.g., several weeks, because of the structure of the system 10 and its sterilization features. The system 10 can be stored appropriately at room temperature, a refrigerated temperature or a frozen temperature, until another dosage is to be withdrawn. With the control system, variable doses of the drug solution can be withdrawn over time merely by programming the system accordingly. This is especially beneficial in oncology practice where drug dosages are often required in non-standard amounts. In addition, containers 12 containing different drug solutions can be readily changed in the system 10.

Furthermore, the container system 10 can be used with any number of different drugs. Different drugs contained in separate containers 12 can be placed in the dispensing/sterilization device to allow for multiple doses to be withdrawn over time. The system also affords the ease of use of syringe/needle technology, favored by pharmacists, yet with the sterility assurance of, for example, the FDA approved sterile access device conventionally used in blood banks. The present system is more efficient and less labor intensive than this sterile access device.

The multi-dose container system 10 also provides considerable flexibility in the delivery of drugs to patients. The system can be provided with a sterile, empty container, permitting the hospital pharmacy the flexibility to use it for any admixture desired and prepared in the

pharmacy. Alternatively, a drug manufacturer could provide a line of drugs, premixed in the containers 12 and installed in the system 10, using either terminal sterilization or aseptic filling techniques, and provide the final product to the customer. A line of oncology drugs is particularly attractive to use in the present system 10 because: (1) the typically intravenous nature of the drugs; (2) convenience from the oncologist's perspective because the drug is prepared reconstituted and ready to use; (3) the flexible plastic container 12 protects the user from the dangerous aerosols that are released when oncology drugs are withdrawn from a standard glass vial, attendant with unavoidable pressure differentials created between the container interior and ambient conditions; and (4) oncology drug dosages are often required in non-standard volumes, which can be readily and efficiently prepared using the present system. The flexible nature of the plastic container 12 minimizes pressure build-up within the container 12 preventing dangerous aerosols from being emitted.

A company could use this unique method to package and deliver its drugs as a drug life cycle extension strategy. For example, by packaging a branded drug using the present system 10, the branded drug can be differentiated from other drugs when patent expiration is near. Alternatively, a generic drug company may choose to package its drugs using the present system 10 to differentiate its generic offering.

The present invention can be used in various other applications. For example, biofermentation is useful in the production of numerous products including drugs, chemicals, beverages, and food products. A biofermentation of a flowable material in a reactor is generally susceptible to contaminates from outside the reactor when it is necessary to access the material during fermentation. The present invention is useful in that it allows repeated sterile access to the reactor for the addition of ingredients to the reactor, or for the withdrawal of samples. Biofermentations are useful in several stages of increasing size, from a small shaken flask culture up through a unit containing many thousands of gallons. It can be appreciated that sterile access to the container containing the biofermentation is desirable regardless of the stage.

Another application for the present invention is for the withdrawing of a sample of blood from a container for the testing of the blood for typing, for infectious organisms or vectors, or for other diagnostic testing. The testing of blood intended for transfusion is essential. Often, testing involves withdrawing a sample from a blood bag or other blood

holding mother container. The present invention allows for the sterile sampling of blood without the introduction of live microorganisms to the blood intended for transfusion.

The present invention is also useful for the manufacturing of large scale sterile pharmaceutical liquids. In one embodiment, the first container is a large volume flexible container used as a liner within a steel tank. The steel tank is the container holder and the liner acts as a sterile reactor for the manufacture of pharmacological agents. The liner includes a port assembly which is accessible through an access port in the steel tank. The present invention is then used to sterilely access the pharmacological agent to add ingredients to the container, or to withdraw samples for quality control testing. The container's port assembly has a port tube sealed with a resilient stopper so the container can be repeatedly accessed. This invention is particularly well suited to this application due to the high cost incurred if contamination of a large volume of pharmaceutical product occurs.

While the specific embodiments have been illustrated and described, numerous modifications come to mind without significantly departing from the spirit of the invention, and the scope of protection is only limited by the scope of the accompanying claims.

We claim:

1. A multi-dose container system comprising:

a first container having a port assembly adapted to be pierced by a piercing member of a second container, the first container adapted to hold a flowable material;

a collapsible member positioned around the port assembly, the member adapted to receive the piercing member; and

a sterilization device positioned adjacent the collapsible member and adapted to sterilize the piercing member when positioned within the collapsible member.

2. The system of claim 1, wherein the first container is in the size range of from about 50mL to about one liter.

3. The system of claim 1, wherein the port assembly has a port tube.

4. The system of claim 1, wherein the port assembly is closed by a resilient stopper.

5. The system of claim 5, wherein the resilient stopper is a rubber stopper.

6. The system of claim 1, further comprising a housing positioned about the components of the system.

7. The system of claim 7, further comprising a controller positioned on a wall of the housing and operably connected to the system.

8. The system of claim 1, further comprising a container support connected to the container.

9. The system of claim 1, wherein the sterilization device utilizes ultra-violet light.

10. The system of claim 10, further comprising a plurality of annular-shaped lamps.

11. The system of claim 1, wherein the sterilization device utilizes heat sterilization.

12. The system of claim 1, wherein the second container is a syringe, the syringe having a plunger movable within a syringe barrel.

13. The system of claim 13, further comprising a carriage to support the syringe.

14. The system of claim 13, further comprising a syringe autoholder mechanism.

15. The system of claim 15, further comprising a syringe activator operably coupled to the syringe to move the syringe from a first position wherein the piercing member does not pierce the port assembly to a second position wherein the piercing member pierces the port assembly and is in fluid communication with the first container.

16. The system of claim15, further comprising a plunger activator operably coupled to the syringe to move the syringe plunger.

17. The system of claim 1, wherein the collapsible member includes a bellows assembly.

18. The system of claim 1, wherein the collapsible member has a first end and a second end, wherein the first end is sealingly fit around the port assembly, and the second end is sealed by a septum.

19. The system of claim 19, further comprising a removable cap positioned over the septum.

20. The system of claim 1, further comprising a control mechanism operably connected to the autoholder.

21. The system of claim 21, wherein the control system is adapted to receive data input by an operator.

22. The system of claim 1, wherein the first container is a biofermentation reactor.

23. The system of claim 1, wherein the first container is a blood bag.

24. A system for sterilely accessing a container repeatedly for withdrawal or addition of a fluid to the container comprising:

a first container having a port assembly adapted to be pierced by a piercing member of a second container, the first container adapted to hold a flowable material;

a collapsible member positioned around the port assembly, the member adapted to receive the piercing member; and

a sterilization device positioned adjacent the collapsible member and adapted to sterilize the piercing member when positioned within the collapsible member.

25. A method of withdrawing a drug dose from a multi-dose container system, the method comprising the steps of:

providing a container holding a drug solution, the container having a port;

providing a sterilization device proximal the port;

providing a second container having a piercing member; and

sterilizing the piercing member just before piercing the member into the port.

26. A method according to claim 26, further comprising providing a collapsible member positioned around the piercing member that provides a sterile barrier in which the piercing member is sterilized before piercing the port.

27. A method according to claim 27, wherein the piercing member is sterilized through the collapsible member.

28. A method according to claim 26, wherein the step of sterilizing the piercing member is performed by radiation.

29. A method according to claim 26, wherein the step of sterilizing the piercing member is performed by chemicals.

30. A method according to claim 26, wherein the step of sterilizing the piercing member is performed by heat.

31. A multi-dose container system providing for multiple doses of a drug solution to be withdrawn from the system over an extended period of time, the system comprising:

a container having a port assembly extending from the container, the port assembly having a tube sealed by a plug, the container holding a drug solution;

a collapsible member having a first end opening positioned over the port assembly and a second end opening sealed by a septum, the collapsible member being movable between a first position and a second, collapsed position;

a sterilization device positioned adjacent the collapsible member and adapted to sterilize a needle placed in the collapsible member;

a syringe assembly having a syringe barrel with a needle at one end and a plunger slidable within the syringe barrel, the needle being pierced through the septum and positioned within the collapsible member;

a syringe activator connected to the syringe assembly for moving syringe assembly and the collapsible member from the first position to the second position; and

a plunger activator having an arm connected to the plunger.

32. A container access system providing for repeated sterile access to a flowable material contained in a container including the repeated, sterile addition or withdrawal of a fluid over an extended period of time, the system comprising:

a container having a port assembly extending from the container, the port assembly having a tube sealed by a plug, the container holding a fluid;

a collapsible member having a first end opening positioned over the port assembly and a second end opening sealed by a septum, the collapsible member being movable between a first position and a second, collapsed position;

a sterilization device positioned adjacent the collapsible member and adapted to sterilize a needle placed in the collapsible member;

a syringe assembly having a syringe barrel with a needle at one end and a plunger slidable within the syringe barrel, the needle being pierced through the septum and positioned within the collapsible member;

a syringe activator connected to the syringe assembly for moving syringe assembly and the collapsible member from the first position to the second position; and

a plunger activator having an arm connected to the plunger.

33. A method of withdrawing a drug dose from a multi-dose container system, the method comprising the steps of:

providing a container holding a drug solution, the container having a port;

providing a bellows assembly having a first end opening positioned around the port and a second end opening sealed by a septum;

providing a sterilization device adjacent the bellows assembly;

providing a syringe assembly having a syringe barrel with a needle extending therefrom and a plunger slidable within the syringe barrel;

piercing through the septum with the needle wherein the needle is positioned in the bellows assembly;

activating the sterilization device to sterilize the needle;

collapsing the bellows assembly wherein the needle pierces through the port assembly;

pulling back on the plunger to withdraw drug solution from the container and into the syringe; and

removing the syringe assembly from the container and bellows assembly for delivery to a patient.

34. A method of withdrawing a flowable material from a container system, the method comprising the steps of:

providing a container holding a flowable material, the container having a port;

providing a bellows assembly having a first end opening positioned around the port and a second end opening sealed by a septum;

providing a sterilization device adjacent the bellows assembly;

providing a syringe assembly having a syringe barrel with a needle extending therefrom and a plunger slidable within the syringe barrel;

piercing through the septum with the needle wherein the needle is positioned in the bellows assembly;

activating the sterilization device to sterilize the needle;

collapsing the bellows assembly wherein the needle pierces through the port assembly;

pulling back on the plunger to withdraw flowable material from the container and into the syringe; and

removing the syringe assembly from the container and bellows assembly.

FIG. 1

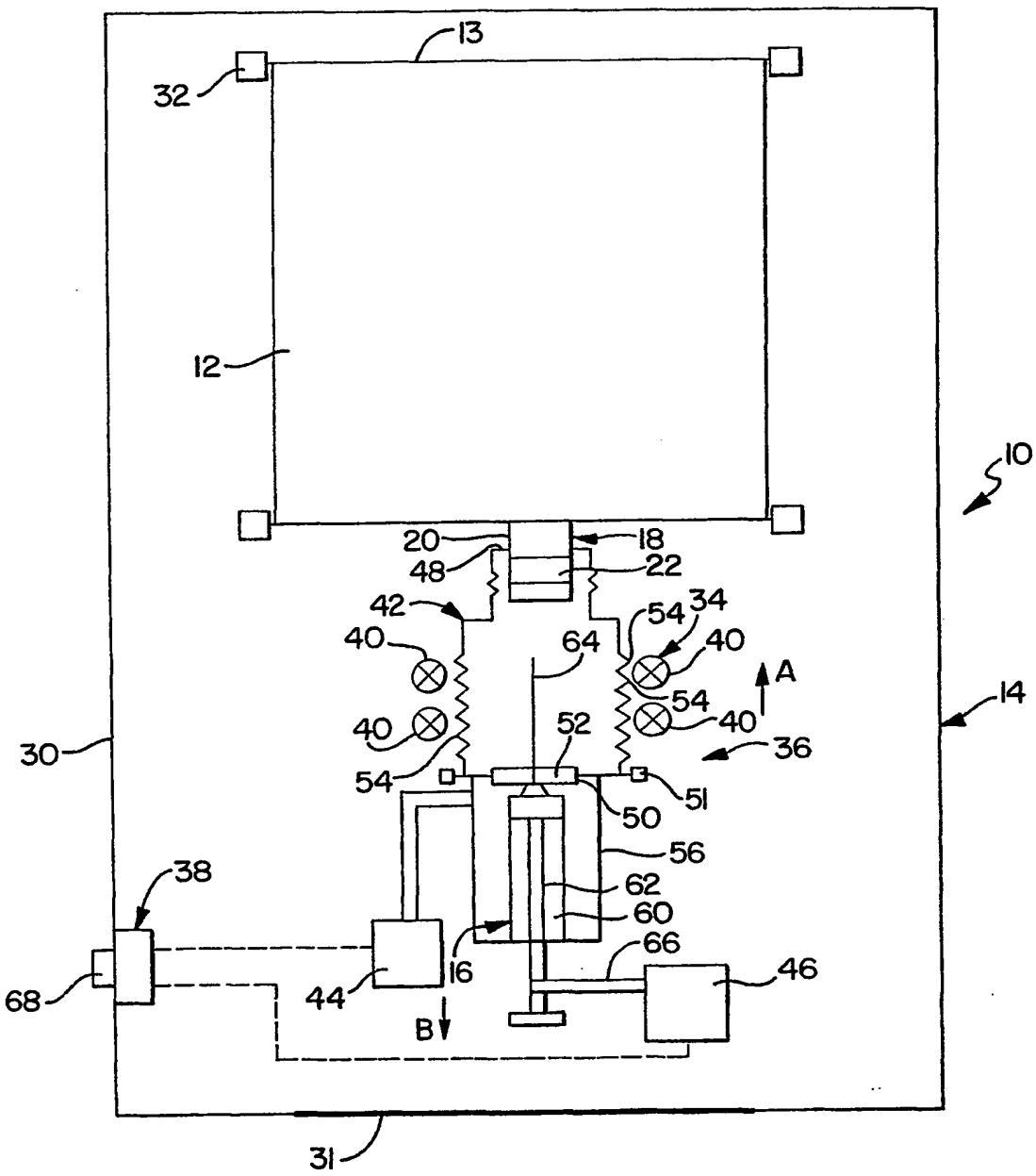
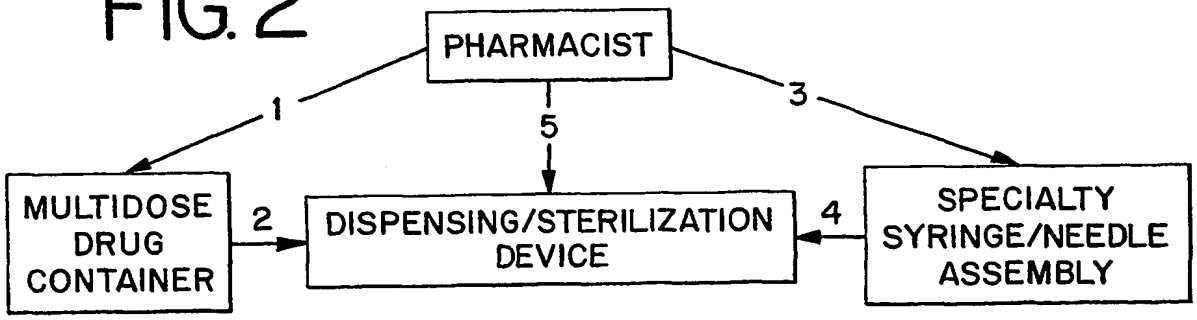


FIG. 2



INTERNATIONAL SEARCH REPORT

International Application
PCT/US 01/42714

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61J1/00 A61L2/00 A61M39/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61J A61L A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 83 02060 A (BAXTER TRAVENOL LAB) 23 June 1983 (1983-06-23) page 8, line 12 - line 22	1-6,8,9, 11,17, 18, 23-26,28
A	page 9, line 34 -page 10, line 6; figures	7,10,12, 19,20, 22,31-34
A	US 5 352 210 A (MARRUCCHI PIERO) 4 October 1994 (1994-10-04) column 8, line 1 - line 4; figures	1-34
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
14 February 2002	21/02/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Cametz, C

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A	WO 85 00979 A (BAXTER TRAVENOL LAB) 14 March 1985 (1985-03-14) page 7, line 29 - line 35 page 11, line 36 - line 40; figures	1-34

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Int[redacted]ional Application No
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